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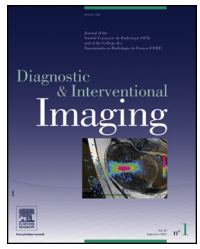

SHORT ORIGINAL ARTICLE /*Neuroradiology*

Subtentorial cerebral nocardiosis in immunocompetent patients: CT and MR imaging findings

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Abstract
Purpose: To describe the clinical presentation and computed tomography (CT) and magnetic resonance imaging (MRI) appearances of subtentorial nocardia cerebral abscesses developing in immunocompetent patients.
Patients and methods: The clinical findings and the results of CT and MRI examinations of three immunocompetent patients with nocardiosis located initially only in the subtentorial region were studied. Three patients underwent CT examination and two patients had MRI.
Results: Clinically, two patients had cerebellar syndrome and the third had meningism with fever. The diagnosis of nocardiosis was bacteriologically confirmed by demonstrating the organism in lumbar puncture fluid in one patient and by an aspiration biopsy of the abscess in the other two. Two of the patients improved under targeted antibiotic therapy whereas the third patient died. The main imaging features of the lesions were a multiloculated appearance with peripheral enhancement after intravenous administration of iodinated contrast material on CT and a multicystic appearance on MRI, with a peripheral hypointense rim on T2-weighted images, a relatively minor mass effect and a multiloculated appearance on gadolinium-chelate enhanced T1-weighted images.
Conclusion: The clinical presentation of cerebral nocardiosis is relatively non-specific. A microcystic lesion surrounded by hypointensity on T2-weighted MR images with a multiloculated pattern after gadolinium chelate administration on T1-weighted MR images in association with a relatively minor mass effect should suggest this diagnosis even if the lesion is single and in the absence of immunosuppression.

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Abscesses due to Nocardia, a Gram-positive filamentous bacteria account for approximately 2% of all cerebral abscess. A single subtentorial location is even rarer, making the diagnosis difficult. Nocardia predominantly affects immunosuppressed patients [1] although it is not particularly rare for immunocompetent patients to be affected by the disease and these patients usually respond well to targeted antibiotic therapy pending that the diagnosis is suggested by the results of imaging examination [2,3]. On the basis of three clinical cases investigated in our institution, we wished to report the clinical presentation and imaging features of subtentorial abscesses due to nocardia in immunocompetent patients.

Case reports

Patient 1

A 64-year-old woman with no remarkable past history developed hypoesthesia on the right side of her face and cerebellar symptoms. MR imaging examination of the brain performed at 1.5 Tesla showed a right cerebellar and middle cerebellar peduncular lesion with homogeneous and hyperintense appearance on fluid attenuated inversion recovery (FLAIR) images and a microcystic appearance surrounded by an peripheral hypointense rim on T2 weighted images (turbo spin echo, repetition time (TR)/echo time (TE): 4059/100 ms). A moderate mass effect was seen (Fig. 1). The lesion showed marked hyperenhancing peripheral rim after intravenous administration (IV) of gadolinium chelate, featuring a target appearance with central cystic area, resulting in a multiloculated appearance. The lesion was hyperintense on diffusion-weighted imaging ($b = 1000\,s/mm^2$, TR/TE: 8300/92 ms), but with no drop in the apparent diffusion coefficient. In this regard, the ADC value was 1.33×10^{-3} mm^2/s, corresponding to increase of 50% compared to the apparently healthy contralateral side. Spectroscopy showed a moderate rise in the choline peak with a choline/NAA radio of close to 1 and no lactate, lipid or amino acid peak. Chest, abdominal and pelvic CT was normal and lumbar puncture was negative. Listeriosis was suspected and empirical therapy was started with amoxicillin, sulfamethoxazole-trimethoprim and corticosteroids, which initially produced some imaging improvement. Six months later, the patient developed headaches and a homonymous hemianopia found to be a second, left occipital, site of disease.

Lumbar puncture demonstrated cerebral nocardiosis, with a positive polymerase chain reaction for Nocardia species. The patient subsequently recovered on antibiotic therapy with imipenem and sulfamethoxazole-trimethoprim.

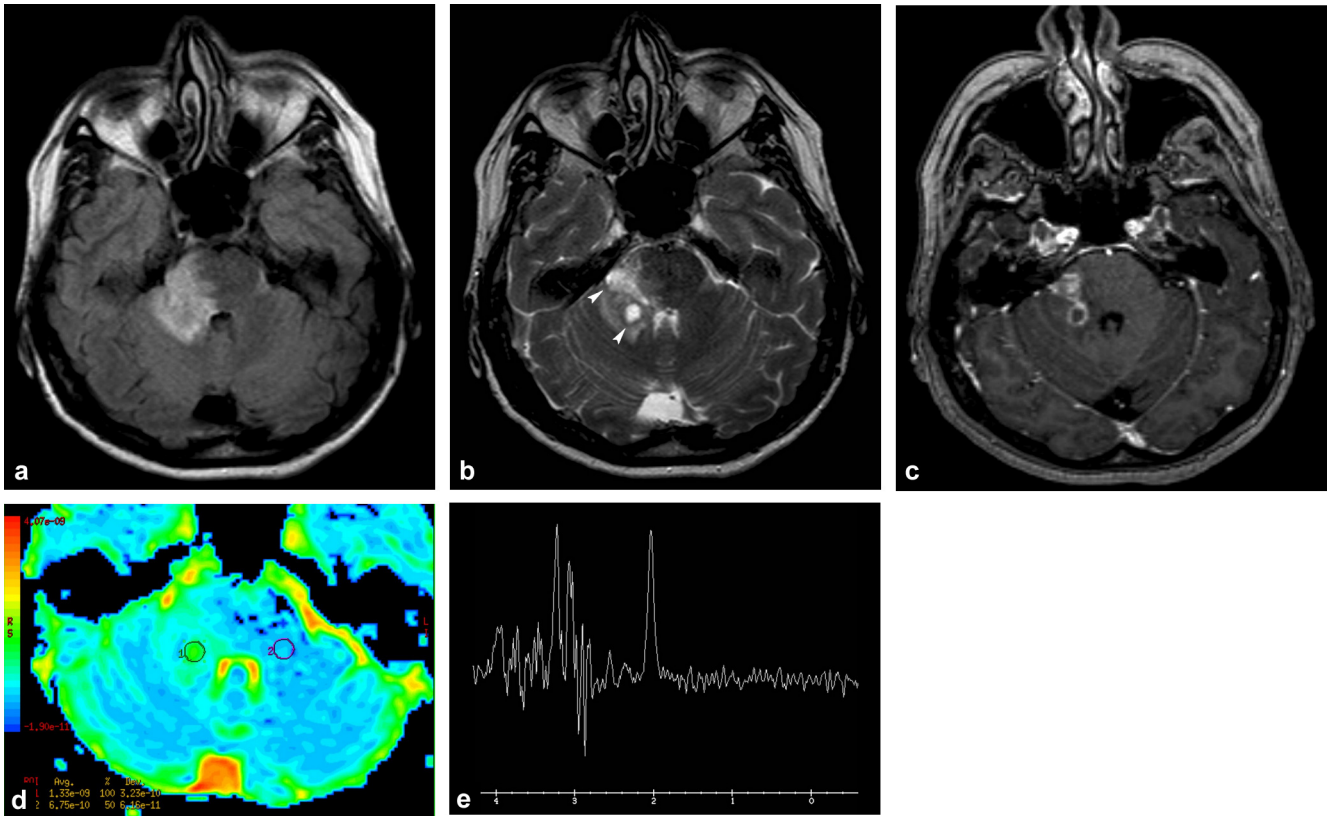

Figure 1. Cerebral MRI in patient 1: a: axial FLAIR image shows middle cerebellar peduncular and right sided cerebellar lesion with a homogeneous hyperintensity; b: T2-weighted TSE axial image (TR/TE: 4059/100 ms) reveals cystic areas exhibiting pronounced hyperintensity with a peripheral hypointense line (arrowheads); c: T1-weighted gradient-echo axial image after IV of gadolinium chelate (TR/TE: 7.1/3.2 ms) shows multiloculated appearance (arrowhead); d: diffusion weighted image ($b = 1000\,s/mm^2$, ADC mapping) shows increased ADC value within the lesion with an ADC of $1.33 \times 10^{-3} mm^2/s$ (region of interest in green); e: spectroscopy (TE = 144 ms) shows moderately raised choline peak, choline/NAA ratio close to 1.

Patient 2

A 51-year-old man with a past history of hypertension developed occipital headaches with cerebellar symptoms occurring on wakening. Before IV, CT showed a hypoattenuating cerebellar lesion in the vermis with a few hyperattenuating areas that partially enhanced peripherally after IV of iodinated contrast material. MRI showed a heterogeneous lesion on T2-weighted (TSE, TR/TE: 6280/94 ms) and FLAIR imaging with a central hypointense area on FLAIR which was hypointense on T2*, thus confirming hemorrhagic changes (Fig. 2). A peripheral hypointense rim was present on T2-weighted images. The lesion enhanced heterogeneously after IV of gadolinium chelate and was multiloculated. Diffusion-weighted MRI ($b = 1000$ s/mm^2, TR/TE: 8000/106 ms) showed a heterogeneous appearance associated with foci of hemorrhage. Perfusion-weighted imaging showed an area of increased perfusion with a blood volume four times greater than that of healthy contralateral areas. It was not possible to determine whether the lesion was a tumour, an abscess or a tumour with abscess. The patient received cefotaxime and corticosteroids but his condition initially deteriorated clinically with an extensive mass effect in the posterior fossa which required a direct neurosurgical approach. The bacteriological results from the samples taken confirmed the presence of *Nocardia farcinica* and the patient's treatment was then changed to sulfamethoxazole-trimethoprim and cefotaxime. However, he deteriorated rapidly and developed an increasing mass effect in the posterior fossa. The patient developed diffuse meningitis and died.

Patient 3

A 68-year-old man with a past history of type II diabetes and hypertrophic cardiomyopathy developed a cerebellar syndrome associated with rapid neurological deterioration. CT revealed a cerebellar lesion in the vermis extending to the left side of the cerebellum, which was multiloculated with a liquid component in its center, enhancing peripherally but with only mild mass effect compared to its size (Fig. 3). The patient had a pacemaker and could therefore not have MRI and the initial assumption made was that of a high grade glial tumor and he received corticosteroids. His neurological status deteriorated rapidly and repeat CT showed an increase in size of the lesion, at which point infection was suggested. Surgical evacuation of the abscess isolated the organism Nocardia species. The patient received sulfamethoxazole-trimethoprim yielding rapid clinical and radiological improvement and he then recovered.

Discussion

Our three cases of cerebral nocardiosis have common symptomatic and imaging features. On conventional MRI, the appearances were mostly those of a lesion containing central multiloculated area made up of cystic cavities displaying pronounced hyperintensity on T2-weighted imaging and hypointensity on T1-weighted imaging. This central portion is surrounded by a hypointense line combined with an extensive area of edema, which is hyperintense on T2-weighted images. The FLAIR images show predominantly homogeneous lesion except for areas of hemorrhagic changes.

The lesion enhances after IV of gadolinium-chelate producing a non-specific annular appearance. On the other hand, the peripheral hypointense annular appearance on the T2-weighted images is more characteristic and is believed to occur as a result of organization of necrotic debris and phagocytosis of the capsule by macrophages [4]. This T2-weighted hypointense rim is also observed in other bacterial and fungal abscesses and is not specific for nocardiosis, but does suggest an infectious cause. A double hypointense rim on T2-weighted images appears to be more specific for Nocardia abscesses [4] and is believed to be explained by the fact that Nocardia grows relatively slowly so that peripheral changes due the host defense against the bacterium, results in a thick capsule [4].

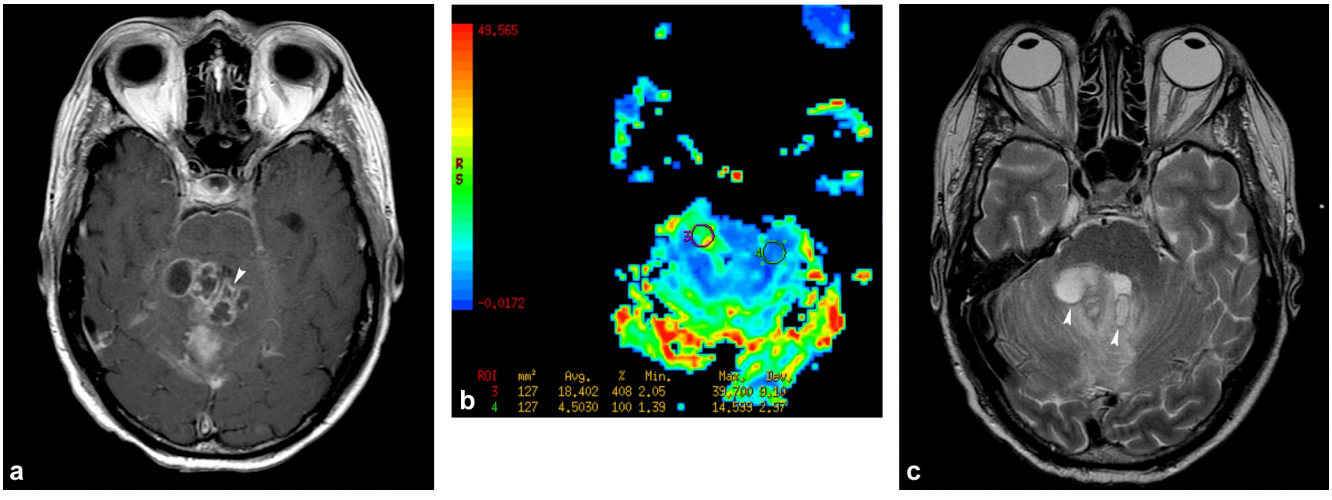

Figure 2. Cerebral MRI in patient 2: a: T1-weighted gradient echo axial image after IV of gadolinium chelate (TR/TE: 20/5 ms) shows a lesion in the vermis with a multiloculated appearance; b: perfusion-weighted image (cerebral blood volume mapping) shows an area of increased perfusion (region of interest shown in violet) with a blood flow four times greater than that of the contralateral healthy area; c: T2-weighted TSE axial image (TR/TE: 6280/94 ms) shows a multicystic appearance with a peripheral hypointense line (arrowheads).

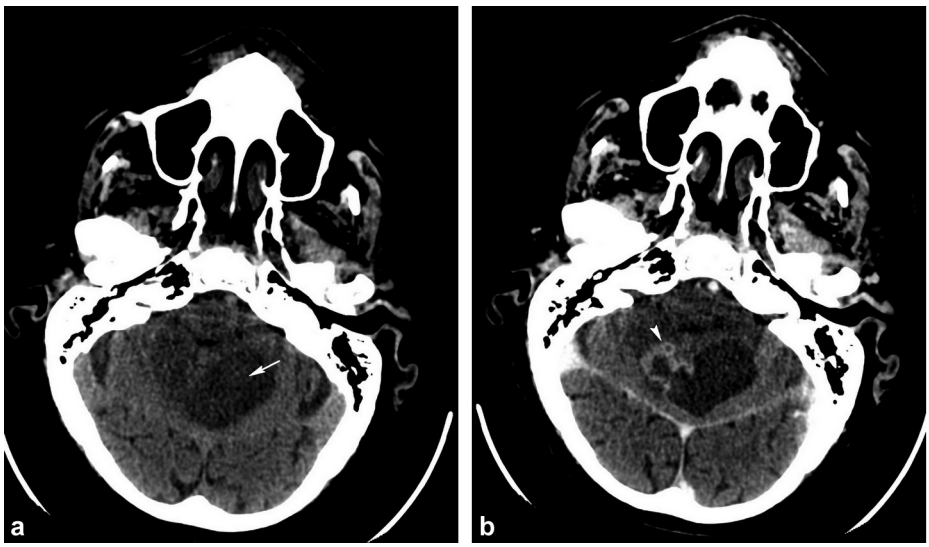

Figure 3. CT scan in patient 3: a: before IV of iodinated contrast material, CT shows a lesion in the superior cerebellar vermis, which is multiloculated with a central portion of water attenuation value (arrow); b: after IV of iodinated contrast material, the lesion shows peripheral enhancement (arrowhead) and mild mass effect.

The multilocular appearance on MRI or CT, with an area of abscess made up of several cystic cavities is also suggestive of the diagnosis of nocardiosis and helps differentiation from abscesses due to pyogenic organisms, which are usually uniloculated. The multiloculated nature of the lesions may be explained by their growth with direct extension of the filaments through tissues [5].

We observed a hyperintense appearance on diffusion weighted imaging in two of our patients with an increased ADC in one and a moderately reduced ADC in the second compared to the contralateral side. Similarly, in the literature Nocardia abscesses appear to display either a similar appearance on diffusion weighted imaging to those of an abscess due to pyogenic organisms, with a reduced ADC [6,7], or an appearance similar that of tuberculosis or toxoplasmosis abscesses with no reduction in diffusion [3].

The main differential diagnosis is that of a tumour, particularly one which is necrotic or cystic in nature and several cases of cerebral nocardiosis treated surgically for suspected high grade glioma have been reported [2]. On imaging, the hypointense line on T2 weighted imaging is not characteristic of a tumour [8] and similarly the mass effect in this case is modest overall compared to the volume of the lesion.

Spectroscopy which was carried out in patient 1 showed a metabolic profile which was non-neoplastic in appearance with no choline peak or increase in lipids. Murray et al. have also reported an immunocompetent patient with supra- and subtentorial nocardiosis lesions with no choline peak [9]. Similarly, Yaakup et al. found no choline peak but did find a lactate peak in an immunocompetent patient [3].

The perfusion weighted MRI images in patient 2 showed increase perfusion of the lesions. This increase in perfusion in the enhanced part of the lesion has also been reported by Cianfoni et al., associated with dilated capsular capillary vessels found histologically in this study [10]. Conversely, in patient 1, no increased perfusion was found, as in the cases reported by Holmes et al. [11,12].

It is important to suggest a diagnosis on imaging as the clinical presentation is usually relatively non-specific. Mamelak et al. reported 131 cases of cerebral nocardiosis and concluded that CT reduced overall mortality from 60 to 37% [1]. Exposure to the organism (usually through earth) is not easily suspected from the clinical enquiry and there is usually no clinical or laboratory evidence of an infectious cause. As in our three patients, fever and a laboratory acute phase reaction are often absent and in addition nocardiosis may develop without immunodeficiency in 42% of patients [5]. The diagnosis is even more difficult in these immunocompetent patients when the clinical background is not suggestive of opportunistic disease and the cerebral involvement may be isolated. However, the distinction between tumour and abscess is essential as corticosteroids may reduce the neoplastic cerebral edema but can cause rapid progression of an abscess resulting in the patient deteriorating or even dying.

Few cases of a single subtentorial site of nocardiosis have been reported by contrast with a majority of supratentorial casea of nocardiosis [1]. Only six [13—18] of the 58 patients (10.3%) with cerebral nocardiosis included in the literature reviewed by Franck et al. had a subtentorial abscess [19] and of the seven cases of subtentorial nocardiosis reported in the literature [13—19], only two [15,17] had a single location in the posterior fossa. The other five had concomitant supratentorial sites of disease. In addition, posterior fossa abscesses are unusual abscess sites in the brain and are usually due to abscesses caused by pyogenic organisms associated with local sites of infection, particularly oto-mastoiditis or secondary sites (paradoxical embolism due to pulmonary arteriovenous fistulae, etc.) [20]. A single subtentorial location of the disease may therefore be a misleading feature.

The definite diagnosis is made by identifying the bacterium in lumbar puncture fluid or from an aspiration biopsy. These procedures can be delayed with subtentorial sites of disease because of the risk of herniation of the amygdala

and it is therefore important to suggest the diagnosis of nocardiosis on imaging in order that the necessary diagnostic samples can be taken as quickly as possible.

Conclusion

In conclusion, cerebral nocardiosis has a relatively non-specific presentation. However, the microcystic appearance on CT and T2-weighted MR imaging surrounded by a peripheral hypointense rim on T2-weighted images with multiloculated contrast enhancement and a mild mass effect should suggest the diagnosis, even if the lesion is single and in the absence of immunosuppression. Identification of the nocardiosis is facilitated if the bacteriologist is informed about the suspected diagnosis as this may be missed on routine tests.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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